

Amendments to the Claims:

This listing of claims replaces all prior versions and listings of claims in the application:

Listing of Claims:

1-20. Cancelled.

21. (Previously presented) A method for constructing a single chain diabody library, the method comprising:

(a) providing a first phage antibody library that encodes single chain antibodies that bind to a first antigen, each member of the library comprising a nucleotide sequence encoding a light chain variable domain and a nucleotide sequence encoding a heavy chain variable domain, wherein the nucleotide sequence encoding the light chain variable domain is connected to the nucleotide sequence encoding the heavy chain variable domain by a first nucleotide linker of 45 to 60 base pairs encoding a peptide linker and comprising a cleavage site for a first restriction enzyme and a cleavage site for a second restriction enzyme that is different from the first restriction enzyme;

(b) providing a second phage antibody library that encodes single chain antibodies that bind to a second antigen, each member of the library comprising (i) a nucleotide sequence encoding a light chain variable domain and (ii) a nucleotide sequence encoding a heavy chain variable domain, wherein the nucleotide sequence of (i) is connected to the nucleotide sequence of (ii) by a second nucleotide linker of 45 to 60 base pairs encoding a peptide linker, and wherein the end of the nucleotide sequence of (i) that is distal to the second nucleotide linker comprises a cleavage site for the first restriction enzyme, and the end of the nucleotide sequence of (ii) that is distal to the second nucleotide linker comprises a cleavage site for the second restriction enzyme;

(c) treating the first library with the two restriction enzymes to cleave the two sites within the first nucleotide linker;

(d) treating the second library with the two restriction enzymes to produce a plurality of fragments, each fragment having a cleaved restriction site at its 5' end and a cleaved restriction site at its 3' end, wherein each fragment comprises the nucleotide sequence of (b)(i) connected to the nucleotide sequence of (b)(ii) via the second nucleotide linker; and
(e) ligating the cleaved product of (c) with the plurality of fragments of (d) to construct a third library of nucleic acids, each encoding a single polypeptide chain comprising both the light and heavy chain variable domains of (a) and the light and heavy chain variable domains of (b), wherein the light and heavy chain variable domains of (b) are inserted between the light and heavy chain variable domains of (a) and are separated from the light and heavy chain variable domains of (a) by a pair of short linkers, each encoded by 6 to 27 base pairs, wherein the lengths of the short linkers are determined by the locations of the cleavage sites for the first and second restriction enzymes in the first nucleotide linker of (a).

22-32. Cancelled.

33. (Previously presented) A method for producing a construct encoding a single chain diabody, the method comprising:

(a) providing a first nucleic acid that encodes a single chain antibody polypeptide that binds to a first antigen and comprises a nucleotide sequence encoding a light chain variable domain and a nucleotide sequence encoding a heavy chain variable domain, wherein the nucleotide sequence encoding the light chain variable domain is connected to the nucleotide sequence encoding the heavy chain variable domain by a first nucleotide linker of 45 to 60 base pairs encoding a peptide linker and comprising a cleavage site for a first restriction enzyme and a cleavage site for a second restriction enzyme that is different from the first restriction enzyme;

(b) providing a second nucleic acid that encodes a single chain antibody polypeptide that binds to a second antigen and comprises (i) a nucleotide sequence encoding a light chain variable domain and (ii) a nucleotide sequence encoding a heavy chain variable domain, wherein the nucleotide sequence of (i) is connected to the nucleotide sequence of (ii) by a second nucleotide linker of 45 to 60 base pairs encoding a peptide linker, and wherein the end of the nucleotide sequence of (i) that is distal to the second nucleotide linker comprises a cleavage site

for the first restriction enzyme, and the end of the nucleotide sequence of (ii) that is distal to the second nucleotide linker comprises a cleavage site for the second restriction enzyme;

(c) treating the first nucleic acid with the two restriction enzymes to cleave the two sites within the first nucleotide linker;

(d) treating the second nucleic acid with the two restriction enzymes to produce a fragment having a cleaved restriction site at its 5' end and a cleaved restriction site at its 3' end, wherein the fragment comprises the nucleotide sequence of (b)(i) connected to the nucleotide sequence of (b)(ii) via the second nucleotide linker; and

(e) ligating the cleaved product of (c) with the fragment of (d) to construct a third nucleic acid encoding a single polypeptide chain comprising both the light and heavy chain variable domains of (a) and the light and heavy chain variable domains of (b), wherein the light and heavy chain variable domains of (b) are inserted between the light and heavy chain variable domains of (a) and are separated from the light and heavy chain variable domains of (a) by a pair of short linkers, each encoded by 6 to 27 base pairs; wherein the lengths of the short linkers are determined by the locations of the cleavage sites for the first and second restriction enzymes in the first nucleotide linker of (a); and wherein the third nucleic acid either is an expression vector or is inserted into an expression vector subsequent to the ligating step.

34-42. Cancelled

43. (Previously presented) A method for constructing an antibody library, the method comprising:

(a) providing a phage antibody library that encodes single chain antibodies that bind to an antigen, each member of the library comprising a first nucleotide sequence encoding a light chain variable domain and a second nucleotide sequence encoding a heavy chain variable domain, both domains being directed against the same antigen, wherein the first nucleotide sequence is connected to the second nucleotide sequence by a nucleotide linker of 45 to 60 base pairs encoding a peptide linker and comprising two or more cleavage sites for a restriction enzyme;

(b) treating the library with the restriction enzyme to cleave the two or more sites

within the nucleotide linker; and

(c) self-ligating the cleaved product of (b) to generate a second antibody library, each member of the second library comprising the first and the second nucleotide sequences joined by a nucleotide linker that is shorter than the nucleotide linker in the library of (a).

44. (Cancelled)

45. (Currently amended) The method of claim 21, wherein the amino acid sequence of the peptide linker of (a) and the amino acid sequence of the peptide linker of (b) each contains one or more copies of the sequence GlyGlyGlyGlySer (SEQ ID NO: 6).

46. (Currently amended) The method of claim 21, wherein the amino acid sequence of the peptide linker of (a) and the amino acid sequence of the peptide linker of (b) each is [GlyGlyGlyGlySer (SEQ ID NO: 6)]_n, wherein n is 3 or 4.

47. (Currently amended) The method of claim 21, wherein the amino acid sequence of the peptide linker of (a) and the amino acid sequence of the peptide linker of (b) each is [GlyGlyGlyGlySer (SEQ ID NO: 6)]₄.

48. (Currently amended) The method of claim 33, wherein the amino acid sequence of the peptide linker of (a) and the amino acid sequence of the peptide linker of (b) each contains one or more copies of the sequence GlyGlyGlyGlySer (SEQ ID NO: 6).

49. (Currently amended) The method of claim 33, wherein the amino acid sequence of the peptide linker of (a) and the amino acid sequence of the peptide linker of (b) each is [GlyGlyGlyGlySer (SEQ ID NO: 6)]_n, wherein n is 3 or 4.

50. (Currently amended) The method of claim 33, wherein the amino acid sequence of the peptide linker of (a) and the amino acid sequence of the peptide linker of (b) each is [GlyGlyGlyGlySer (SEQ ID NO: 6)]₄.

51. (Currently amended) The method of claim 43, wherein the amino acid sequence of the peptide linker contains one or more copies of the sequence GlyGlyGlyGlySer(SEQ ID NO: 6).

52. (Currently amended) The method of claim 43, wherein the amino acid sequence of the peptide linker is [GlyGlyGlyGlySer(SEQ ID NO: 6)]_n, wherein n is 3 or 4.

53. (Currently amended) The method of claim 43, wherein the amino acid sequence of the peptide linker is [GlyGlyGlyGlySer(SEQ ID NO: 6)]₄.